08/302,241
attachment to Paper # 37

```
* * * * * * * * * * * * * * * * * * * * * * * * * * * * * * * * *
  *                  W E L C O M E   T O   T H E                  *
  *          U. S.   P A T E N T   T E X T   F I L E              *
  * * * * * * * * * * * * * * * * * * * * * * * * * * * * * * * * *
=> s glutamine synthetase and amplifi?
          7795 GLUTAMINE
          2275 SYNTHETASE
           148 GLUTAMINE SYNTHETASE
                 (GLUTAMINE(W)SYNTHETASE)
        218023 AMPLIFI?
L1          74 GLUTAMINE SYNTHETASE AND AMPLIFI?
=> s l1 and vector?
         58362 VECTOR?
L2          69 L1 AND VECTOR?
=> d l2,1-69
```

1. 5,644,036, Jul. 1, 1997, Purified immunoglobulin; Paul Ian Nicholas Ramage, et al., 530/412; 435/69.6; 530/413, 416, 417 [IMAGE AVAILABLE]

2. 5,641,670, Jun. 24, 1997, Protein production and protein delivery; Douglas A. Treco, et al., 435/254.11, 320.1 [IMAGE AVAILABLE]

3. 5,641,664, Jun. 24, 1997, Process for transforming monocotyledonous plants; Kathleen D'Halluin, et al., 435/172.3, 69.1, 252.2; 800/200, 205, DIG.56; 935/52, 67 [IMAGE AVAILABLE]

4. 5,639,948, Jun. 17, 1997, Stamen-specific promoters from rice; Frank Michiels, et al., 800/205; 47/58, DIG.1; 435/172.1, 172.3, 414, 419; 536/23.2, 23.6, 24.1; 935/35, 36, 67 [IMAGE AVAILABLE]

5. 5,639,275, Jun. 17, 1997, Delivery of biologically active molecules using cells contained in biocompatible immunoisolatory capsules; Edward E. Baetge, et al., 604/891.1; 424/93.1, 93.2, 422, 424; 435/172.3 [IMAGE AVAILABLE]

6. 5,637,489, Jun. 10, 1997, Phosphinothricin-resistance gene, and its use; Eckhard Strauch, et al., 435/172.3 [IMAGE AVAILABLE]

7. 5,635,381, Jun. 3, 1997, Agrobacterium bacteria capable of site-specific recombination; Paul J. J. Hooykaas, et al., 435/172.3, 71.2, 199, 252.2, 252.3, 320.1, 419; 536/23.72 [IMAGE AVAILABLE]

8. 5,631,158, May 20, 1997, Methods and compositions for high protein production from non-native DNA; Haimanti Dorai, et al., 435/172.3, 70.21, 172.2, 252.3, 320.1; 530/387.3, 867; 536/23.53, 23.72, 24.1 [IMAGE AVAILABLE]

9. 5,631,133, May 20, 1997, Transition in transcriptional activation by intracellular hormone receptors at the tumor stage of dermal fibrosarcoma development; Douglas Hanahan, et al., 435/6, 69.4, 172.1 [IMAGE AVAILABLE]

10. 5,627,047, May 6, 1997, Astrocyte-specific transcription of human genes; Michael Brenner, et al., 435/69.1, 69.7, 320.1, 325, 354, 368; 536/23.4, 23.5, 24.1 [IMAGE AVAILABLE]

11. 5,627,033, May 6, 1997, Mammalian expression **vectors**; John M. Smith, et al., 435/6, 91.41, 172.3, 320.1, 325, 358, 365 [IMAGE

AVAILABLE]

12. 5,623,053, Apr. 22, 1997, Soluble mammal-derived Fc receptor which binds at a pH ranging from about 5.5 to 6.5 and releases at a pH ranging from about 7.5 to 8.5; Louis N. Gastinel, et al., 530/350; 435/69.1 [IMAGE AVAILABLE]

13. 5,616,487, Apr. 1, 1997, Stabilized retrovirus compositions; Bernhard O. Palsson, et al., 435/235.1, 172.3 [IMAGE AVAILABLE]

14. 5,614,385, Mar. 25, 1997, Methods and compositions for high protein production from recombinant DNA; Hermann Oppermann, et al., 435/69.4, 254.2, 325 [IMAGE AVAILABLE]

15. 5,612,213, Mar. 18, 1997, Method of selecting mammalian cell lines having improved productivity; Sham Y. Chan, 435/6, 69.1, 320.1, 325, 366, 369 [IMAGE AVAILABLE]

16. 5,605,814, Feb. 25, 1997, DNA encoding human prostaglandin receptor EP2; Mark Abramovitz, et al., 435/69.1, 252.3, 254.11, 320.1, 366, 369, 372; 536/23.5 [IMAGE AVAILABLE]

17. 5,605,690, Feb. 25, 1997, Methods of lowering active TNF-.alpha. levels in mammals using tumor necrosis factor receptor; Cindy A. Jacobs, et al., 424/134.1; 435/69.7; 514/12, 825; 530/350, 387.3, 866, 868 [IMAGE AVAILABLE]

18. 5,604,115, Feb. 18, 1997, Liver enriched transcription factor; Frances M. Sladek, et al., 435/69.1, 252.3, 254.11, 320.1, 325, 348; 536/23.5 [IMAGE AVAILABLE]

19. 5,595,896, Jan. 21, 1997, Expression of heterologous genes in transgenic plants and plant cells using plant asparagine synthetase promoters; Gloria M. Coruzzi, et al., 435/172.3, 69.1; 800/205 [IMAGE AVAILABLE]

20. 5,591,639, Jan. 7, 1997, Recombinant DNA expression **vectors**; Christopher R. Bebbington, 435/320.1, 172.3; 536/24.1, 24.2 [IMAGE AVAILABLE]

21. 5,591,630, Jan. 7, 1997, Monoclonal antibodies that bind interleukin-15 receptors; Dirk M. Anderson, et al., 435/331, 334; 530/388.22 [IMAGE AVAILABLE]

22. 5,589,610, Dec. 31, 1996, Stamen-specific promoters from corn; Marc De Beuckeleer, et al., 800/205; 435/172.3, 320.1, 412, 414, 419; 536/22.1, 23.6, 24.1, 24.3, 24.5; 800/250, DIG.56; 935/6, 30, 35 [IMAGE AVAILABLE]

23. 5,589,374, Dec. 31, 1996, Diabetogene rad: a type II diabetes specific gene; C. Ronald Kahn, et al., 435/69.1, 252.3, 320.1; 536/23.2, 23.5 [IMAGE AVAILABLE]

24. 5,585,237, Dec. 17, 1996, Methods and compositions for high protein production from recombinant DNA; Hermann Oppermann, et al., 435/6, 172.3, 325, 350, 353, 358 [IMAGE AVAILABLE]

25. 5,578,461, Nov. 26, 1996, Gene manipulation and expression using

genomic elements; Stephen Sherwin, et al., 435/69.1, 172.3, 244, 320.1; 536/23.1, 24.1; 935/28, 33, 55 [IMAGE AVAILABLE]

26. 5,567,862, Oct. 22, 1996, Synthetic insecticidal crystal protein gene; Michael J. Adang, et al., 800/205; 435/69.1, 418; 800/250 [IMAGE AVAILABLE]

27. 5,567,600, Oct. 22, 1996, Synthetic insecticidal crystal protein gene; Michael J. Adang, et al., 536/23.71; 435/69.1, 172.3 [IMAGE AVAILABLE]

28. 5,561,236, Oct. 1, 1996, Genetically engineered plant cells and plants exhibiting resistance to **glutamine** **synthetase** inhibitors, DNA fragments and recombinants for use in the production of said cells and plants; Jan Leemans, et al., 800/205; 435/172.3, 418; 536/23.1, 23.2, 23.7; 935/75 [IMAGE AVAILABLE]

29. 5,561,053, Oct. 1, 1996, Method for selecting high-expressing host cells; Craig W. Crowley, 435/69.1, 172.3, 320.1, 358; 536/23.2 [IMAGE AVAILABLE]

30. 5,559,220, Sep. 24, 1996, Gene encoding acetyl-coenzyme A carboxylase; Paul G. Roessler, et al., 536/23.6; 435/69.1, 134, 172.3, 197, 252.3, 257.2, 320.1, 418; 536/23.2 [IMAGE AVAILABLE]

31. 5,545,723, Aug. 13, 1996, Muteins of IFN-.beta.; Susan E. Goelz, et al., 424/85.6; 435/69.51, 252.3, 320.1; 514/12; 530/351; 536/23.52 [IMAGE AVAILABLE]

32. 5,545,545, Aug. 13, 1996, Lysine-insensitive maize dihydrodipicolinic acid synthase; Burle G. Gengenbach, et al., 435/172.3, 412; 530/376; 536/23.6; 800/205, DIG.56, DIG.70 [IMAGE AVAILABLE]

33. 5,545,405, Aug. 13, 1996, Method for treating a mammal suffering from cancer with a cho-glycosylated antibody; Martin J. Page, 424/133.1, 130.1, 143.1, 172.1, 174.1; 435/70.3, 71.1, 320.1; 530/387.1, 388.1, 388.22, 388.73, 388.75, 389.1, 389.6, 389.7 [IMAGE AVAILABLE]

34. 5,545,404, Aug. 13, 1996, Method for treating a mammal suffering from a T-cell medicated disorder with a CHO-Glycosylated antibody; Martin J. Page, 424/133.1, 130.1, 143.1, 173.1, 174.1; 435/70.3, 71.1, 320.1; 530/387.1, 388.22, 388.73, 388.75, 388.8, 389.1, 389.6, 389.7 [IMAGE AVAILABLE]

35. 5,545,403, Aug. 13, 1996, Method for treating a mammal by administering a CHO-glycosylated antibody; Martin J. Page, 424/133.1, 130.1, 135.1, 136.1, 138.1, 143.1, 147.1, 150.1, 159.1, 172.1, 174.1; 435/70.3, 71.1, 320.1; 530/387.1, 388.1, 388.22, 388.73, 388.75, 389.1, 389.6, 389.7 [IMAGE AVAILABLE]

36. 5,541,310, Jul. 30, 1996, Herbicide resistant plants; Eric R. Ward, et al., 536/23.6; 435/252.3, 320.1, 348, 418 [IMAGE AVAILABLE]

37. 5,532,142, Jul. 2, 1996, Method of isolation and purification of fusion polypeptides; Stephen A. Johnston, et al., 435/69.1, 69.7, 219 [IMAGE AVAILABLE]

38. 5,516,652, May 14, 1996, DNA encoding prostaglandin receptor IP;

Mark Abramovitz, et al., 435/69.1, 252.3, 254.11, 320.1, 365; 530/350; 536/23.1 [IMAGE AVAILABLE]

39. 5,500,361, Mar. 19, 1996, .beta.-ketoacyl-ACP synthetase II genes from plants; Anthony J. Kinney, 435/172.3, 69.1, 71.1; 536/23.6; 800/205, 250, 255, DIG.69 [IMAGE AVAILABLE]

40. 5,496,934, Mar. 5, 1996, Nucleic acids encoding a cellulose binding domain; Oded Shoseyov, et al., 536/23.7; 435/252.3, 320.1; 536/23.1, 24.33 [IMAGE AVAILABLE]

41. 5,495,007, Feb. 27, 1996, Phloem-specific promoter; Gary A. Thompson, et al., 536/24.1; 435/172.3, 320.1; 536/23.6; 800/205; 935/35 [IMAGE AVAILABLE]

42. 5,468,845, Nov. 21, 1995, Antibodies to osteogenic proteins; Hermann Oppermann, et al., 530/387.9, 350 [IMAGE AVAILABLE]

43. 5,464,937, Nov. 7, 1995, Type II Interleukin-1 receptors; John E. Sims, et al., 530/350 [IMAGE AVAILABLE]

44. 5,457,182, Oct. 10, 1995, FK-506 cytosolic binding protein, FKBP12.6; Gregory J. Wiederrecht, et al., 530/402; 435/7.8, 69.1, 233; 530/350, 413 [IMAGE AVAILABLE]

45. 5,447,913, Sep. 5, 1995, Therapeutic uses of bactericidal/permeability-increasing protein dimer products; William S. Ammons, et al., 514/12, 21; 530/350 [IMAGE AVAILABLE]

46. 5,427,940, Jun. 27, 1995, Engineered cells producing insulin in response to glucose; Christopher B. Newgard, 435/366; 424/520; 435/4, 6, 69.1, 172.1, 172.2, 172.3, 320.1; 530/303, 350, 389.2, 397 [IMAGE AVAILABLE]

47. 5,420,247, May 30, 1995, Leukemia inhibitory factor receptors and fusion proteins; David P. Gearing, et al., 530/350, 387.3, 388.23, 391.1, 402; 536/23.51 [IMAGE AVAILABLE]

48. 5,420,019, May 30, 1995, Stable bactericidal/permeability-increasing protein muteins; Georgia Theofan, et al., 435/69.1, 252.3, 320.1; 530/350; 536/23.5 [IMAGE AVAILABLE]

49. 5,395,760, Mar. 7, 1995, DNA encoding tumor necrosis factor-.alpha. and -.beta. receptors; Craig A. Smith, et al., 435/365; 424/85.1; 435/69.4, 172.3; 530/351, 388.23; 536/23.51 [IMAGE AVAILABLE]

50. 5,391,725, Feb. 21, 1995, Organ-specific plant promoter sequences; Gloria M. Coruzzi, et al., 536/24.1; 435/69.1, 172.3, 320.1; 800/205; 935/35, 36 [IMAGE AVAILABLE]

51. 5,380,831, Jan. 10, 1995, Synthetic insecticidal crystal protein gene; Michael J. Adang, et al., 536/23.71; 435/69.1, 172.3; 800/205 [IMAGE AVAILABLE]

52. 5,354,557, Oct. 11, 1994, Osteogenic devices; Hermann Oppermann, et al., 424/423, 422, 424, 426 [IMAGE AVAILABLE]

53. 5,350,683, Sep. 27, 1994, DNA encoding type II interleukin-1

receptors; John E. Sims, et al., 435/69.1, 252.3, 320.1; 530/350; 536/23.5 [IMAGE AVAILABLE]

54. 5,284,755, Feb. 8, 1994, DNA encoding leukemia inhibitory factor receptors; David P. Gearing, et al., 435/69.1, 69.7, 252.3, 320.1; 536/23.4, 23.5 [IMAGE AVAILABLE]

55. 5,276,268, Jan. 4, 1994, Phosphinothricin-resistance gene, and its use; Eckhard Strauch, et al., 800/205; 435/172.3, 252.3, 418; 536/23.7; 800/255, DIG.43; 935/67 [IMAGE AVAILABLE]

56. 5,273,894, Dec. 28, 1993, Phosphinothricin-resistance gene, and its use; Eckhard Strauch, et al., 435/129, 128, 172.3, 193, 252.3, 418; 536/23.2, 23.7 [IMAGE AVAILABLE]

57. 5,266,683, Nov. 30, 1993, Osteogenic proteins; Hermann Oppermann, et al., 530/326, 327, 328, 350, 395, 840 [IMAGE AVAILABLE]

58. 5,256,558, Oct. 26, 1993, Gene encoding plant asparagine synthetase; Gloria M. Coruzzi, et al., 435/252.33, 172.3, 252.3, 320.1; 536/23.2, 24.1 [IMAGE AVAILABLE]

59. 5,145,777, Sep. 8, 1992, Plant cells resistant to herbicidal **glutamine** **synthetase** inhibitors; Howard M. Goodman, et al., 435/172.3, 69.1, 320.1, 418; 504/206, 319, 320, 322; 536/23.2, 23.6; 800/200, 205, 255; 935/33, 35 [IMAGE AVAILABLE]

60. 5,137,816, Aug. 11, 1992, Rhizobial diagnostic probes and rhizobium trifolii nifH promoters; Barry G. Rolfe, et al., 435/172.3, 252.2, 252.3, 320.1, 878; 536/23.6, 23.71; 935/41, 72 [IMAGE AVAILABLE]

61. 5,122,464, Jun. 16, 1992, Method for dominant selection in eucaryotic cells; Richard H. Wilson, et al., 435/172.3, 320.1 [IMAGE AVAILABLE]

62. 5,098,838, Mar. 24, 1992, Expression of wild type and mutant **glutamine** **synthetase** in foreign hosts; Howard Goodman, et al., 435/183, 252.3, 252.33, 320.1; 536/23.2, 23.6; 935/10, 27, 29, 66, 67, 72, 73 [IMAGE AVAILABLE]

63. 5,043,270, Aug. 27, 1991, Intronic overexpression **vectors**; John M. Abrams, et al., 435/69.1, 172.3, 320.1, 358; 536/23.2, 23.5; 935/34, 61, 66, 70, 71, 79, 84 [IMAGE AVAILABLE]

64. 5,008,194, Apr. 16, 1991, nifH promoters of Bradyrhizobium; Barry G. Rolfe, et al., 435/172.3, 252.2, 252.3, 320.1; 536/23.6, 24.1; 935/6, 35, 41 [IMAGE AVAILABLE]

65. 5,001,061, Mar. 19, 1991, nifD promoter of Bradyrhizobium; Barry G. Rolfe, et al., 435/172.3, 252.2, 252.3, 320.1; 536/23.1, 23.6, 24.2; 935/6, 35, 41 [IMAGE AVAILABLE]

66. 4,975,374, Dec. 4, 1990, Expression of wild type and mutant **glutamine** **synthetase** in foreign hosts; Howard Goodman, et al., 435/172.3, 183, 252.3, 252.33; 536/23.2, 23.6; 935/14, 29, 30, 73 [IMAGE AVAILABLE]

67. 4,956,288, Sep. 11, 1990, Method for producing cells containing

stably integrated foreign DNA at a high copy number, the cells produced by this method, and the use of these cells to produce the polypeptides coded for by the foreign DNA; James G. Barsoum, 435/172.3, 69.1, 70.1, 71.1, 172.1, 252.3; 935/16, 33, 52 [IMAGE AVAILABLE]

68. 4,803,165, Feb. 7, 1989, Nif promoter of fast-growing rhizobium japonicum; Edward R. Appelbaum, 435/172.3, 69.1, 252.2, 252.33, 320.1; 536/23.6, 23.7, 23.71, 24.1; 935/29, 30, 41, 56, 64, 67, 72 [IMAGE AVAILABLE]

69. 4,782,022, Nov. 1, 1988, Nitrogen fixation regulator genes; Alfred Puhler, et al., 435/172.3, 252.2, 252.33, 320.1; 536/23.2, 23.6, 23.71, 24.1; 930/200; 935/29, 56, 72 [IMAGE AVAILABLE]

=> d fro,11,20

US PAT NO: 5,627,033 [IMAGE AVAILABLE] L2: 11 of 69
DATE ISSUED: May 6, 1997
TITLE: Mammalian expression **vectors**
INVENTOR: John M. Smith, Columbia Heights, MN
John E. Humphrey, Maple Grove, MN
Monica L. Tsang, North Oaks, MN
James A. Weatherbee, North Oaks, MN
ASSIGNEE: Research & Diagnostics Systems, Inc., Minneapolis, MN (U.S. corp.)
APPL-NO: 08/411,490
DATE FILED: Mar. 28, 1995
INT-CL: [6] C12Q 1/68
US-CL-ISSUED: 435/6, 91.41, 172.3, 320.1, 325, 358, 365
US-CL-CURRENT: 435/6, 91.41, 172.3, 320.1, 325, 358, 365
SEARCH-FLD: 435/6, 172.3, 91.1, 320.1, 91.41
REF-CITED:

U.S. PATENT DOCUMENTS

5,149,636	9/1992	Axel et al.	435/69.1
5,266,683	11/1993	Oppermann et al.	530/326

FOREIGN PATENT DOCUMENTS

62011096	1/1987	Japan	C12N 15/00
04179485	6/1992	Japan	C12N 15/65

OTHER PUBLICATIONS

R.J. Kaufman, "Selection and Coamplification of Heterologous Genes in Mammalian Cells", in Methods in Enzymology, 185:537-566 (1990).
R.J. Kaufman, "Vectors Used for Expression in Mammalian Cells" in Methods in Enzymology, 185:487-511 (1990).
Kim et al., (Abstract) "Effects of Multiple Mutations at the Conserved TATA Sequence of Bacteriophage SP6 Promoter on Transcription Activity", Biochem. and Mol. Biol. Int. 31(1):153-9 (1993).
Mulligan and Berg (Proc. Natl. Acad. Sci., 78:2072-2076 (1981)).
Pauly, et al., "The Initiation of Accuracy of the SV40 Early Transcription is Determined by the Functional Domains of Two TATA elements", Nucleic Acids Res., 20(5):975-982 (1992).
"Expression of Proteins" Chapter 16, Expression of Cloned Genes in Cultured Mammalian Cells, in Molecular Cloning: A Laboratory Manual, J. Sambrook ed, 2nd ed., pp. 16.3-16.31 (1989).
Japanese Publ. No. 04-179485 (Abstract) DIALOG File 347 (JAPIO).
WPI Acc. No. 92-263665/32 (Abstract) DIALOG File 351 (Derwent WPI).
Niwa et al., "Efficient Selection for High-expression Transfectants with

a Novel Eukaryotic Vector", Gene 108:193-199 (1991).
ART-UNIT: 185
PRIM-EXMR: James Ketter
LEGAL-REP: Fredrickson & Byron, P.A.

ABSTRACT:
A **vector** system that allows the rapid and effective screening of recombinant constructs. The **vector** system includes a marker protein useful for identifying transfected cell lines, wherein the promoter used to express the marker protein has be substantially weakened in comparison to its corresponding wild type form.
29 Claims, No Drawings

US PAT NO: 5,591,639 [IMAGE AVAILABLE] L2: 20 of 69
DATE ISSUED: Jan. 7, 1997
TITLE: Recombinant DNA expression **vectors**
INVENTOR: Christopher R. Bebbington, Windsor, United Kingdom
ASSIGNEE: Celltech Ltd, Berkshire, United Kingdom (foreign corp.)
APPL-NO: 08/300,063
DATE FILED: Sep. 2, 1994
REL-US-DATA: Continuation of Ser. No. 896,797, Jun. 9, 1992, abandoned, which is a continuation of Ser. No. 339,615, Apr. 28, 1989, abandoned.
FRN-PRIOR: United Kingdom 8717430 Jul. 23, 1987
INT-CL: [6] C12N 15/00; C07H 21/04
US-CL-ISSUED: 435/320.1, 172.3; 536/24.1, 24.2
US-CL-CURRENT: 435/320.1, 172.3; 536/24.1, 24.2
SEARCH-FLD: 536/24.1, 24.2; 435/172.3, 320.1
REF-CITED:

U.S. PATENT DOCUMENTS

4,769,326	9/1988	Rutter	435/68

FOREIGN PATENT DOCUMENTS

173177	3/1986	European Patent Office
173552	3/1986	European Patent Office
260148	3/1988	European Patent Office

OTHER PUBLICATIONS

Boshart et al in Sequence Specificity in Transcript & Translation pp. 511-520 The Strong Enhance-Element . . . 1985.
Foecking et al Gene 45:101-105. 1986.
Gruss et al PNAS 76(9):4317-4321. 1979.
Hamer et al Cell 17:725. 1979.
Mulligan et al Nature 277:108. 1979.
Spaete et al J of Virl 56(1):135, 1985.
Nelsen et al Mol. Cell Biol 7(11):4125, 1987.
Slenkey et al J of Virl 49(1):190, 1984.
Gene, vol. 38, No. 1/3.1985, Elsevier Biomedical Press, (Amsterdam, NL) F. Pasleau et al.:"Growth hormone gene expression in eukaryotic cells directed by the Rous sarcoma virus long terminal repeat or cytomegalovirus immediate--early promoter", pp. 227-232;see p. 228, second col.
Journal of Virology, vol. 56, No. 1, Oct. 1985, American Society for Microbiology (US) R. R. Spaete et al.:"Regulation of cytomegalovirus gene expression:.alpha. and .beta. promoters are trans activated by viral functions in permissive human fibroblasts" pp. 135-143, see p. 136, last five lines and first paragraph of p. 137 (cited in the

application).
Wong et al., "Human GM-CSF: Molecular Cloning of the Complementary DNA and Purification of the Natural and Recombinant Proteins", Science, v. 228, pp. 810-15, May 1985.
Simonsen et al., "Isolation and expression of an altered mouse dihydrofolate reductase cDNA", Proc. Natl. Acad. Sci. (USA), vol. 80, pp. 2495-2499, 1983.
Kaufman et al., "Amplification and Expression of Sequences Cotransfected with a Modular Dihydrofolate Reductase Complementary DNA Gene", J. Mol. Biol., v. 159 pp. 601-621, 1982.
Gething et al., "Cell-surface expression of influenza haemagglutinin from a cloned DNA copy of the RNA gene", Nature, vol. 293, pp. 620-625, 1981.
McLean et al., "Cloning and expression of human lecithin-cholesterol acyltransferase cDNA", Proc. Natl. Acad. Sci. (USA), vol. 83, pp. 2335-2339, 1986.
Leonard et al., "Molecular cloning and expression of cDNAs for the human interleukin-2 receptor", Nature, vol. 311, pp. 626-631, 1984.
Gray et al., "Expression of

TITLE: DNA encoding tumor necrosis factor-.alpha. and -.beta. receptors

13. 5,391,725, Feb. 21, 1995, Organ-specific plant promoter sequences; Gloria M. Coruzzi, et al., 536/24.1; 435/69.1, 172.3, 320.1; 800/205; 935/35, 36 [IMAGE AVAILABLE]

US PAT NO: 5,391,725 [IMAGE AVAILABLE] L2: 13 of 35
TITLE: Organ-specific plant promoter sequences

14. 5,380,831, Jan. 10, 1995, Synthetic insecticidal crystal protein gene; Michael J. Adang, et al., 536/23.71; 435/69.1, 172.3; 800/205 [IMAGE AVAILABLE]

US PAT NO: 5,380,831 [IMAGE AVAILABLE] L2: 14 of 35
TITLE: Synthetic insecticidal crystal protein gene

15. 5,354,557, Oct. 11, 1994, Osteogenic devices; Hermann Oppermann, et al., 424/423, 422, 424, 426 [IMAGE AVAILABLE]

US PAT NO: 5,354,557 [IMAGE AVAILABLE] L2: 15 of 35
TITLE: Osteogenic devices

16. 5,350,683, Sep. 27, 1994, DNA encoding type II interleukin-1 receptors; John E. Sims, et al., 435/69.1, 252.3, 320.1; 530/350; 536/23.5 [IMAGE AVAILABLE]

US PAT NO: 5,350,683 [IMAGE AVAILABLE] L2: 16 of 35
TITLE: DNA encoding type II interleukin-1 receptors

17. 5,316,938, May 31, 1994, Defined media for serum-free tissue culture; Michael J. Keen, et al., 435/240.31, 71.1, 240.2, 240.25 [IMAGE AVAILABLE]

US PAT NO: 5,316,938 [IMAGE AVAILABLE] L2: 17 of 35
TITLE: Defined media for serum-free tissue culture

18. 5,284,755, Feb. 8, 1994, DNA encoding leukemia inhibitory factor receptors; David P. Gearing, et al., 435/69.1, 69.7, 252.3, 320.1; 536/23.4, 23.5 [IMAGE AVAILABLE]

US PAT NO: 5,284,755 [IMAGE AVAILABLE] L2: 18 of 35
TITLE: DNA encoding leukemia inhibitory factor receptors

19. 5,276,268, Jan. 4, 1994, Phosphinothricin-resistance gene, and its use; Eckhard Strauch, et al., 800/205; 435/172.3, 240.4, 252.3; 536/23.7; 800/255, DIG.43; 935/67 [IMAGE AVAILABLE]

US PAT NO: 5,276,268 [IMAGE AVAILABLE] L2: 19 of 35
TITLE: Phosphinothricin-resistance gene, and its use

20. 5,276,145, Jan. 4, 1994, Methods and compositions; purified preparation of neural progenitor regulatory factor; Jane E. Bottenstein, 530/399, 350 [IMAGE AVAILABLE]

US PAT NO: 5,276,145 [IMAGE AVAILABLE] L2: 20 of 35
TITLE: Methods and compositions; purified preparation of neural progenitor regulatory factor

21. 5,273,894, Dec. 28, 1993, Phosphinothricin-resistance gene, and its use; Eckhard Strauch, et al., 435/129, 128, 172.3, 193, 240.4, 252.3; 536/23.2, 23.7 [IMAGE AVAILABLE]

US PAT NO: 5,273,894 [IMAGE AVAILABLE] L2: 21 of 35
TITLE: Phosphinothricin-resistance gene, and its use

22. 5,266,683, Nov. 30, 1993, Osteogenic proteins; Hermann Oppermann, et al., 530/326, 327, 328, 350, 395, 840 [IMAGE AVAILABLE]

US PAT NO: 5,266,683 [IMAGE AVAILABLE] L2: 22 of 35
TITLE: Osteogenic proteins

23. 5,256,558, Oct. 26, 1993, Gene encoding plant asparagine synthetase; Gloria M. Coruzzi, et al., 435/240.1, 172.3, 252.3, 252.33, 320.1; 536/23.2, 24.1 [IMAGE AVAILABLE]

US PAT NO: 5,256,558 [IMAGE AVAILABLE] L2: 23 of 35
TITLE: Gene encoding plant asparagine synthetase

24. 5,145,777, Sep. 8, 1992, Plant cells resistant to herbicidal **glutamine** **synthetase** inhibitors; Howard M. Goodman, et al., 435/172.3, 69.1, 240.4, 320.1; 504/206, 319, 320, 322; 536/23.2, 23.6; 800/200, 205, 255; 935/33, 35 [IMAGE AVAILABLE]

US PAT NO: 5,145,777 [IMAGE AVAILABLE] L2: 24 of 35
TITLE: Plant cells resistant to herbicidal **glutamine** **synthetase** inhibitors

25. 5,137,816, Aug. 11, 1992, Rhizobial diagnostic probes and rhizobium trifolii nifH promoters; Barry G. Rolfe, et al., 435/172.3, 252.2, 252.3, 320.1, 878; 536/23.6, 23.71; 935/41, 72 [IMAGE AVAILABLE]

US PAT NO: 5,137,816 [IMAGE AVAILABLE] L2: 25 of 35
TITLE: Rhizobial diagnostic probes and rhizobium trifolii nifH

promoters

26. 5,122,464, Jun. 16, 1992, Method for dominant selection in eucaryotic cells; Richard H. Wilson, et al., 435/172.3, 320.1 [IMAGE AVAILABLE]

US PAT NO: 5,122,464 [IMAGE AVAILABLE] L2: 26 of 35
TITLE: Method for dominant selection in eucaryotic cells

27. 5,098,838, Mar. 24, 1992, Expression of wild type and mutant **glutamine** **synthetase** in foreign hosts; Howard Goodman, et al., 435/183, 252.3, 252.33, 320.1; 536/23.2, 23.6; 935/10, 27, 29, 66, 67, 72, 73 [IMAGE AVAILABLE]

US PAT NO: 5,098,838 [IMAGE AVAILABLE] L2: 27 of 35
TITLE: Expression of wild type and mutant **glutamine** **synthetase** in foreign hosts

28. 5,043,270, Aug. 27, 1991, Intronic overexpression vectors; John M. Abrams, et al., 435/69.1, 172.3, 240.1, 320.1; 536/23.2, 23.5; 935/34, 61, 66, 70, 71, 79, 84 [IMAGE AVAILABLE]

US PAT NO: 5,043,270 [IMAGE AVAILABLE] L2: 28 of 35

TITLE: Intronic overexpression vectors

29. 5,008,194, Apr. 16, 1991, nifH promoters of Bradyrhizobium; Barry G. Rolfe, et al., 435/172.3, 252.2, 252.3, 320.1; 536/23.6, 24.1; 935/6, 35, 41 [IMAGE AVAILABLE]

US PAT NO: 5,008,194 [IMAGE AVAILABLE] L2: 29 of 35
TITLE: nifH promoters of Bradyrhizobium

30. 5,001,061, Mar. 19, 1991, nifD promoter of Bradyrhizobium; Barry G. Rolfe, et al., 435/172.3, 252.2, 252.3, 320.1; 536/23.1, 23.6, 24.2; 935/6, 35, 41 [IMAGE AVAILABLE]

US PAT NO: 5,001,061 [IMAGE AVAILABLE] L2: 30 of 35
TITLE: nifD promoter of Bradyrhizobium

31. 4,975,374, Dec. 4, 1990, Expression of wild type and mutant **glutamine** **synthetase** in foreign hosts; Howard Goodman, et al., 435/172.3, 183, 252.3, 252.33; 536/23.2, 23.6; 935/14, 29, 30, 73 [IMAGE AVAILABLE]

US PAT NO: 4,975,374 [IMAGE AVAILABLE] L2: 31 of 35
TITLE: Expression of wild type and mutant **glutamine**

synthetase in foreign hosts

32. 4,956,288, Sep. 11, 1990, Method for producing cells containing stably integrated foreign DNA at a high copy number, the cells produced by this method, and the use of these cells to produce the polypeptides coded for by the foreign DNA; James G. Barsoum, 435/172.3, 69.1, 70.1, 71.1, 172.1, 252.3; 935/16, 33, 52 [IMAGE AVAILABLE]

US PAT NO: 4,956,288 [IMAGE AVAILABLE] L2: 32 of 35
TITLE: Method for producing cells containing stably integrated foreign DNA at a high copy number, the cells produced by this method, and the use of these cells to produce the polypeptides coded for by the foreign DNA

33. 4,923,796, May 8, 1990, Method for the quantitative enzymatic determination of ADP; Ulfert Deneke, et al., 435/15, 16, 26, 805, 810 [IMAGE AVAILABLE]

US PAT NO: 4,923,796 [IMAGE AVAILABLE] L2: 33 of 35
TITLE: Method for the quantitative enzymatic determination of ADP

34. 4,803,165, Feb. 7, 1989, Nif promoter of fast-growing rhizobium japonicum; Edward R. Appelbaum, 435/172.3, 69.1, 252.2, 252.33, 320.1; 536/23.6, 23.7, 23.71, 24.1; 935/29, 30, 41, 56, 64, 67, 72 [IMAGE AVAILABLE]

US PAT NO: 4,803,165 [IMAGE AVAILABLE] L2: 34 of 35
TITLE: Nif promoter of fast-growing rhizobium japonicum

35. 4,782,022, Nov. 1, 1988, Nitrogen fixation regulator genes; Alfred Puhler, et al., 435/172.3, 252.2, 252.33, 320.1; 536/23.2, 23.6, 23.71, 24.1; 930/200; 935/29, 56, 72 [IMAGE AVAILABLE]

US PAT NO: 4,782,022 [IMAGE AVAILABLE] L2: 35 of 35
TITLE: Nitrogen fixation regulator genes
=> d fro,27,31

US PAT NO: 5,098,838 [IMAGE AVAILABLE] L2: 27 of 35
DATE ISSUED: Mar. 24, 1992
TITLE: Expression of wild type and mutant **glutamine** **synthetase** in foreign hosts
INVENTOR: Howard Goodman, Newton, MA
Shiladitya DasSarma, Amherst, MA
Edmund Tischer, Palo Alto, CA
Theresa K. Peterman, Cambridge, MA
ASSIGNEE: The General Hospital Corporation, Boston, MA (U.S. corp.)

DISCL-DATE: Dec. 4, 2007
APPL-NO: 07/556,434
DATE FILED: Jul. 24, 1990
REL-US-DATA: Continuation of Ser. No. 10,612, Feb. 4, 1987, Pat. No. 4,975,374, which is a continuation-in-part of Ser. No. 840,744, Mar. 18, 1986, abandoned, and a continuation-in-part of Ser. No. 906,984, Sep. 15, 1986, abandoned.
INT-CL: [5] C12N 9/00; C12N 15/29; C12N 15/70; C12N 15/84
US-CL-ISSUED: 435/183, 320.1, 252.3, 252.33; 536/27; 935/10, 27, 29, 66, 67, 72, 73
US-CL-CURRENT: 435/183, 252.3, 252.33, 320.1; 536/23.2, 23.6; 935/10, 27, 29, 66, 67, 72, 73
SEARCH-FLD: 435/320, 69.1-69.9, 172.1-172.3, 252.3-252.35, 320.1, 183
REF-CITED:

U.S. PATENT DOCUMENTS

4,594,323	6/1986	Csonka et al.	435/107
4,975,374	12/1990	Goodman et al.	435/172.3

OTHER PUBLICATIONS

DasSarma, S. et al., Science 232:1242-1244 (1986).
Cullimore, J. V. et al., J. Mol. Appl. Genet. 2:589-599 (1984).
Donn, G. et al., J. Mol. Appl. Genet. 2:621-635 (1984).
Scolnik, P. A. et al., J. Bacteriol. 155:180-185 (1983).
Fisher, R. et al., Proc. Natl. Acad. Sci. USA 78:3393-3397 (1981).
Sanders, P. G. et al., EMBO J. 3:65-71 (1984).
Young, A. P. et al., J. Biol. Chem. 258:11260-11266 (1983).
Miller, E. S. et al., J. Biol. Chem. 256:11307-11312 (1981).
Leason, M. et al., Phytochemistry 21:855-857 (1982).
Lara, M. et al., Plant Physiol. 76:1019-1023 (1984).
Tingey, S. V. et al., EMBO J. 6:1-9 (1987).
Botstein, D. et al., Science 229:1193-1201 (1985).
Coulondre et al., J. Mol. Biol. 117:525-567 (1977).
European Search Report for Application (EP 87103936.8) which corresponds to parent case.
Tingey, S. V. et al., Plant Physiol. 84:366-373 (1987).
Baima, S. et al., Carlsberg Res. Commun. 54:1-9 (1989).
Tischer, E. et al., Mol. Gen. Genet. 203:221-229 (1986).
Sambrook, J. et al., Moleular Cloning: A Laboratory Manual, Cold Spring Harbor Laboratory Press 1989, pp. 1.85-1.86.
Gebhardt, C. et al., EMBO J. 5:1425-1435 (1986).
ART-UNIT: 185
PRIM-EXMR: Richard A. Schwartz
ASST-EXMR: William W. Moore
LEGAL-REP: Sterne, Kessler, Goldstein & Fox

ABSTRACT:

The invention relates to a mutant **glutamine** **synthetase** (GS) enzyme which is resistant to inhibition by herbicidal GS inhibitors, such as phosphinothricin (PPT), genetic sequences coding therefor, plants cells and prokaryotes transformed with the genetic sequences, and herbicidal GS inhibitor-resistant plant cells and plants.

18 Claims, 20 Drawing Figures

US PAT NO: 4,975,374 [IMAGE AVAILABLE] L2: 31 of 35
DATE ISSUED: Dec. 4, 1990
TITLE: Expression of wild type and mutant **glutamine** **synthetase** in foreign hosts
INVENTOR: Howard Goodman, Newton, MA
Shiladitya DasSarma, Amherst, MA
Edmund Tischer, Palo Alto, CA
Theresa K. Peterman, Cambridge, MA
ASSIGNEE: The General Hospital Corporation, Boston, MA (U.S. corp.)
APPL-NO: 07/010,612
DATE FILED: Feb. 4, 1987
INT-CL: [5] C12N 15/00; C12N 9/00; C12N 1/20; C07H 15/12
US-CL-ISSUED: 435/172.3, 183, 252.3, 252.33, 320; 536/27; 935/14, 29, 30, 73
US-CL-CURRENT: 435/172.3, 183, 252.3, 252.33; 536/23.2, 23.6; 935/14, 29, 30, 73
SEARCH-FLD: 435/183, 240.46, 252.33, 320; 536/27; 935/14
REF-CITED:

U.S. PATENT DOCUMENTS

4,594,323	6/1986	Csonka et al.	435/107

FOREIGN PATENT DOCUMENTS

86/02097	4/1986	World Intellectual Property Organization	19/34

OTHER PUBLICATIONS

Tingey, S. V. et al., EMBO J. 6:1-9 (1987).
Tingsey, S. V. et al., Plant Physiol. 84:366-373 (1987).
Gebhardt, C. et al., EMBO J. 5:1429-1435 (1986).
DasSarma et al., Science 232:1242-1244 (1986).
Cullimore et al., J. Mol. Appl. Gen. 2:589-599 (1984).
Donn et al., J. Mol. Appl. Gen. 2:621-635 (1984).
Scolnik et al., J. Bacteriol. 155:180-185 (1983).
Fisher et al., Proc. Natl. Acad. Sci. U.S.A. 78:3393-3397 (1981).
Sanders et al., EMBO J. 3:65-71 (1984).
Young et al., J. Biol. Chem. 258:11260-11266 (1983).
Miller et al., J. Biol. Chem. 256:11307-11312 (1981).
Leason et al., Phytochem. 21:855-857 (1982).
Lara et al., Plant Physiol. 76:1019-1023 (1984).
Tingey et al., EMBO J. 6:1-9 (1987).

Botstein et al., Science 229:1193-1201 (1985).
Coulondre et al., J. Mol. Biol. 117:525-575 (1977).
European Search Report for Corresponding Application EPO 87103936.
ART-UNIT: 185
PRIM-EXMR: Thomas D. Mays
LEGAL-REP: Saidman, Sterne, Kessler & Goldstein

ABSTRACT:
The invention relates to a mutant **glutamine** **synthetase** (GS) enzyme which is resistant to inhibition by herbicidal GS inhibitors, such as phosphinothricin (PPT), genetic sequences coding therefor, plants cells and prokaryotes transformed with the genetic sequences, and herbicidal GS inhibitor-resistant plant cells and plants.
30 Claims, 16 Drawing Figures
=> d 27,clms

US PAT NO: 5,098,838 [IMAGE AVAILABLE] L2: 27 of 35

CLAIMS:

CLMS(1)

What is claimed is:

1. A mutant angiosperm **glutamine** **synthetase** enzyme which is resistant to inhibition by a herbicidal **glutamine** **synthetase** inhibitor.

CLMS(2)

2. The mutant angiosperm **glutamine** **synthetase** enzyme of claim 1 which is resistant to inhibition by a herbicidal **glutamine** **synthetase** inhibitor, wherein said enzyme lacks the four native N-terminal amino acid residues 2 to 5, inclusive.

CLMS(3)

3. The mutant angiosperm **glutamine** **synthetase** enzyme of claim 1, wherein said inhibitor is phosphinothricin.

CLMS(4)

4. A nucleic acid molecule coding for a mutant angiosperm **glutamine** **synthetase** enzyme which is resistant to inhibition by a herbicidal **glutamine** **synthetase** inhibitor, wherein said nucleic acid sequence further comprises an ATG codon prior to the codon for the first N-terminal amino acid residue.

CLMS(5)

5. A recombinant DNA molecule comprising a nucleotide sequence coding for a mutant angiosperm **glutamine** **synthetase** enzyme which is resistant to inhibition by a herbicidal **glutamine** **synthetase** inhibitor.

CLMS(6)

6. The recombinant DNA molecule of claim 5, which is a plasmid.

CLMS(7)

7. The recombinant DNA molecule of claim 5, wherein said nucleotide sequence is in operable linkage with a prokaryotic origin of replication, wherein when a prokaryote is transformed with said plasmid, said plasmid replicates.

CLMS(8)

8. The plasmid of claim 7, which is the Ti plasmid of Agrobacterium tumefaciens.

CLMS(9)

9. The recombinant DNA molecule of claim 7, wherein said nucleotide sequence is in further operable linkage with a transcription promoter capable of expressing said **glutamine** **synthetase** sequence in an angiosperm cell.

CLMS(10)

10. A plasmid comprising a prokaryotic origin of replication, a prokaryotic promoter, and a nucleotide sequence coding for a mutant angiosperm **glutamine** **synthetase** enzyme which is resistant to inhibition by a herbicidal **glutamine** **synthetase** inhibitor, wherein when a prokaryotic host is transformed with said plasmid, said plasmid replicates, and said enzyme is expressible.

CLMS(11)

11. A host cell transformed by the recombinant DNA molecule of claim 5.

CLMS(12)

12. The host cell of claim 11, which is a prokaryotic microorganism.

CLMS(13)

13. A prokaryotic microorganism transformed with a recombinant DNA molecule comprising a nucleotide sequence coding for a mutant angiosperm **glutamine** **synthetase** enzyme which is resistant to inhibition by a herbicidal **glutamine** **synthetase** inhibitor.

CLMS(14)

14. The prokaryotic microorganism of claim 13, wherein said recombinant DNA molecule is a plasmid.

CLMS(15)

15. The prokaryotic microorganism of claim 13, which is a bacterium which, in its untransformed state, is incapable of producing functional wild type bacterial **glutamine** **synthetase**.

CLMS(16)

16. The prokaryote of claim 15, which is a mutant bacterium which, in its untransformed state, exhibits diminished **glutamine** **synthetase** activity in comparison to the wild type bacterium.

CLMS(17)

17. The prokaryotic microorganism of any one of claims 13-16 which is E. coli.

CLMS(18)

18. The host cell of claim 11, which is an angiosperm cell.
=>